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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,242	12/06/2000	David M. Kranz	89-99	8588

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GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER

GUZO, DAVID

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 09/06/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/731,242

Applicant(s)

KRANZ ET AL.

Examiner

David Guzo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-10, 13, 14 and 24-103 is/are pending in the application.
- 4a) Of the above claim(s) 6-10, 13, 14, 24-37 and 58-103 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Detailed Action

Applicant's election with traverse of claims corresponding to Group VI, new claims 38-57, in Paper No. 11 is acknowledged. The traversal is on the ground(s) that several of the groups are classified in the same class/subclass. This is not found persuasive because a search of the subject matter of each group in the non-patent literature would involve separate searches that would not be co-extensive and would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-10, 13-14, 24-37 and 58-103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

It is noted that applicants' response to the restriction requirement mailed 3/19/02 included cancellation of some of the originally presented claims that were subject to the restriction requirement and addition of new claims 25-103. The new claims encompass several patentably distinct inventions, including elected claims 38-57, that could be included in the original restriction groups. The breakdown of the restriction groupings for the new claims is as follows:

Claims 25-37, 70-75 are included in original Group I.

Claims 58-63, are included in original Group III

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Claims 64-69, are included in Group IV

Claims 76-83, 99 are included in Group VIII

Claims 84-89, are included in Group VII

Claims 90-91, 94-95 can be included in Groups IV and V

Claims 92-93, are included in Group V

Claim 96-98, 100-101, can be included in Groups III-V.

Claims 102-103, are included in Group II.

The rationale for restriction is as recited in the Restriction Requirement mailed 3/19/02.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patten et al. in view of Dau et al. and Reinherz et al.

Applicants recite soluble mutant T cell receptors (TCRs) having high affinity for a ligand (which may be a peptide/MHC ligand) and having one or more mutations in the CDR3 α or CDR3 β .

Patten et al. (cited above) teaches mutating TCRs in order to improve the affinity of TCRs. Patten et al. does not teach specifically mutating the CDR3 α and CDR3 β region of the TCR or the generation of soluble TCRs.

Dau et al. (U.S. Patent 6,087,096, issued 7/11/00, filed 11/13/95, see whole document, particularly column 1, lines 41-67 and Example 7) recites mutant TCRs having one or more mutations in the CDR regions (CDR3 α and CDR3 β) wherein the ligand of said TCR is a peptide/MHC ligand and methods of identifying said mutants. Dau et al. teaches that mutations in the CDR3 α and CDR3 β are important in ligand binding specificity. Dau et al. does not recite soluble TCR mutants.

Reinherz et al. (cited above) teaches the generation of soluble TCRs and the desirability of generating soluble TCRs as probes to identify antigen/MHC complexes *in vivo*, including those responsible for autoimmune diseases (paragraph bridging columns 5-6).

The Patten et al. reference deals with mutating TCRs in order to increase the affinity of the TCR. Since Dau et al. teaches that the CDR3 α and β regions are involved in binding of the TCR to the antigen/MHC ligand, it would have been obvious to the ordinary skilled artisan, seeking to choose a region of the TCR to mutate in order to

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change the affinity of the molecule, to choose to mutate regions involved with ligand binding (the TCR CDR3 α - β regions). It would have been obvious to produce the TCR in a soluble form because Reinherz et al. teaches the desirability of producing soluble TCRs for potential therapeutic uses in the treatment of autoimmune diseases. The ordinary skilled artisan, seeking to generate soluble TCRs having higher affinity for a ligand and having one or more mutations in the CDR3 α - β , would have been motivated to combine the teachings of Patten et al. on the generation of mutant TCRs so as to improve the affinity of said TCRs for ligands of interest with the teachings of Dau et al. on the importance of mutations in the CDR3 α - β regions of the TCRs in regulating binding of the TCR to the ligand (which is usually a peptide/MHC ligand) and the teachings of Reinherz et al. on the desirability of generating soluble TCRs as therapeutic agents for the treatment of autoimmune diseases *in vivo* in order to mutate TCRs in a region known to be involved in ligand binding (the CDR3 α - β regions) and render them soluble for the desired effect of using them as therapeutic agents for treatment of autoimmune diseases wherein the mutated TCRs bind more effectively to the antigen/MHC complexes on antigen presenting cells *in vivo* and hence prevent activation of autoreactive T cell clones (as taught by Reinherz et al.). Given the teachings of the cited art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in making the soluble recombinant high affinity TCRs.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 (and dependent claims) are vague in the recitation of the phrase "having high affinity" for a ligand. The use of relative terminology such as "high affinity" without a definition of this terminology in the specification or a standard for comparison or a recitation of a dissociation constant renders the metes and bounds of the claimed subject matter indefinite.

Claims 38-39, 48 and 49 (and dependent claims) are vague in that there are no units of measure associated with the dissociation constants. It is unclear how these numbers are calculated.

Claim 54 (and dependent claims) are vague in the recitation of the term "mutant high affinity TCR". Applicants define the term "high affinity TCR" as an engineered TCR having a higher affinity for a ligand than the wild type TCR; however, since applicants recite a "mutant" high affinity TCR, it is unclear if the engineered TCR has been mutagenized in an additional fashion or whether the term "mutant" simply refers to the engineered TCR.

No Claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be submitted directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
September 1, 2002

DAVID GUZO
PRIMARY EXAMINER
